UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/520,031	08/15/2005	Matthew Marton	9301-159	9370

20583 7590 11/28/2007

JONES DAY
222 EAST 41ST ST
NEW YORK, NY 10017

EXAMINER	
KIM, YOUNG J	
ART UNIT	**PAPER NUMBER**
1637	

MAIL DATE	DELIVERY MODE
11/28/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/520,031	MARTON ET AL.	
	Examiner	Art Unit	
	Young J. Kim	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 September 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5-10,37-40 and 42-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-10,37-40 and 42-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/11/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election of Group II, consisting of claims 5-10, 37-39, 40, 42-46 in the reply filed on September 11, 2007 is acknowledged. In addition, it is acknowledged that the newly added claims 47-54 belong to the elected invention of Group II and will be examined herewith. Lastly, election of species (A) quality control probes of species (ii) which embraces probes comprising different predetermined binding sequence; and (B) biopolymers of species (i), being nucleic acids. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Preliminary Remark

Claims 1-4, 11-36, and 41 are canceled.

Claims 47-54 are new.

Information Disclosure Statement

The IDS received on September 11, 2007 is acknowledged.

Claim Objections

Applicant is advised that should claims 47-53 be found allowable, claims 5, 7, and 42-46 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof.

Claims 5 and 47 appear to cover the same breadth[1]. Claims 42 and 48 are verbatim. Claims 43-46 and claims 48-52 are verbatim. Claim 7 and claim 53 are verbatim.

When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one

[1] See comment made under 112, 2nd paragraph for claim 47 for clarification.

claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6, 8-10, 37-40, and 45-54 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 6 is indefinite for the following reasons.

Claim 6 recites that at least some of quality control probes differ from other of said quality control probes in the length of said first sequence, but recites that these first sequences can be a number ranging from ***0***. Since the claim predefines (based on Applicants' election) that all of the quality control probes have the ***same*** predetermined binding sequences, it is unclear how the length of some of these quality control probes can be different if there are **no** first sequence appended thereto. For the purpose of prosecution, the first sequence can be a number ranging from 1 to N monomers, wherein N is greater or equal to 2.

Claims 8-10 and 37-39 are indefinite by way of their dependency on claim 6.

Claim 8 recites the phrase, "two of said two or more quality control probes."

The parent claim 6 clearly recites that there are two types of quality control probes – the ones with first sequences in addition to the predetermined binding sequences and ones without.

Therefore, it becomes confusing which of the quality control probes the limitation is referring to.

Claims 38, 40, 45, 51, and 54 define that the quality control probes are arranged in a periodicity having the variable of, "P" but assigns the number of nozzles the same variable, "P." Therefore, the phrase which recites, "where P is a whole number equal to or greater than 1," becomes confusing as to which of the two (periodicity or number of nozzles) it is referencing to.

Claims 39, 46, and 52 are indefinite for analogous reasons.

Claim 47 is indefinite because the claims at one point recites the phrase, "said plurality of control probes comprising (i) the same predetermined binding sequence..." then later recites that the same "said control probes consists of said predetermined binding sequence."

It is confusing whether the control probes "comprises" or "consists" of a predetermined binding sequence.

Claims 48-53 are indefinite by way of their dependency on claim 47.

For the purpose of prosecution, the control probes is interpreted as "comprising" predetermined binding sequence. Claim duplication objection is made based on this interpretation.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 5, 6, 9, 42, 47, 48, and 54 are rejected under 35 U.S.C. 102(b) as being anticipated by Hubbell et al. (U.S. Patent No. 6,130,046, issued October 10, 2000).

Hubbell et al. disclose a method of determining the quality of the synthesis of an array, said method comprising the steps of:

a) contacting a positionally-addressable biopolymer array which comprises a substrate to which are attached a plurality of different biopolymer probes (column 1, lines 29-39), said different biopolymer probes being situated at different positions on said substrate (Figure 11) and being product of a step-by-step synthesis of said different biopolymer probes on said substrate (column 6, lines 6-10), said plurality of different biopolymer probes comprising a plurality of control probes comprising the same predetermined binding sequence (column 6, lines 52-65), the synthesis of said predetermined binding sequence in each said quality control probe having been initiated during said step-by-step synthesis at sequential cycles of synthesis (column 10, lines 14-18), wherein said sample comprises a binding partner that binds said predetermined binding sequence (column 11, lines 7-12[2]);

b) detecting or measuring binding between two or more of said quality control probes and said binding partner in the sample (column 11, lines 16-21);

c) comparing binding of said two or more of said quality control probes, so as to determine whether a synthesis error had occurred (column 11, lines 20-21 and 40-49), thereby clearly anticipating claims 5, 9, 42, 47, and 48.

With regard to claim 6, Hubbell et al. anticipate the invention as claimed when the first sequence is interpreted with zero being the integer.

With regard to claim 54, it is submitted that how the array is synthesized (i.e., by an inkjet) has no patentable weight as the method employs an array which is already synthesized. Since the array synthesized by Hubbell et al. anticipates the array of claim 54, the claim is anticipated.

Therefore, Hubbell et al. anticipate the invention as claimed.

---

[2] The fact that hybridization pattern is observed with the control probes evidences the fact that a sample comprising a

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 7, 8, 10, 43, 49, and 53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hubbell et al. (U.S. Patent No. 6,130,046, issued October 10, 2000) in view of Lockhart et al. (U.S. Patent No. 6,040,138, issued March 21, 2000).

The teachings of Hubbell et al. have been already discussed above.

Hubbell et al. do not explicitly disclose that the comparison of the control probes involve the determination of binding ratio of two or more quality control probes, wherein said binding ratio is determined by amount of binding of a first of said two quality control probes divided by the amount of binding of a second of said two quality control probes, wherein said binding ratio is being between 0.5 and 2.0 indicates the absence of said synthesis defect.

Hubbell et al. do not explicitly disclose that the sample comprises a total cellular RNA or mRNA from one or more cells, wherein said binding partner is not expressed by said one or more cells.

Lockhart et al. disclose that microarrays are useful in detecting target nucleic acids, such as those derived from a sample comprising cellular RNA or mRNA (column 2, lines 56-58).

---

binding partner that binds said controls probes were present.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Hubbell et al. with the teachings of Lockhart et al., thereby arriving at the invention as claimed for the following reasons.

With regard to the determination of the binding ratio, Hubbell et al. disclose a clear awareness of one of ordinary skill in the art for various way of determining whether the synthesis defect occurred or not by comparing the intensities of the control probes.

In particular, the artisans state:

> "a mean intensities of all the control probes is calculated. By intensity it is meant the measured hybridization affinity of the control probe. Cycle intensity differences ("CIDS") are also calculated at step 481. A cycle intensity difference is the difference between the median of the intensity of all probes that were formed without utilizing a cycle and the median of the intensity of all probes that were formed utilizing the cycle....If a CID is greater than 40% of the mean of the intensities of all the control probes at step 483, the probe synthesis is determined to be unacceptable." (column 11, lines 50-64)

While Hubbell et al. do not explicitly employ the intensity ratio calculation recited in the instant claims, it is submitted that such calculation is deemed obvious and well within the purview of the one of ordinary skill in the art for the following reasons.

The determination of the binding ratio claimed by instant claims takes the ratio of the intensities of the first and the second control probe. If the both control probes were without defect, in an ideal setting, there would not be any differences in the hybridization intensities between the two control probes, resulting in the ratio of 1. However, one of ordinary skill in the art would have clearly recognized that hybridization experimentation cannot be replicated with identical conditions with identical results, and thus, one of ordinary skill in the art would have allowed some acceptable range, allowing for the ratio to be less or greater than 1.

Comparing the intensities of two control probes by taking their ratio for determining differences is rudimentarily employed in statistical analysis and thus, it is respectfully submitted that one of ordinary skill in the art would have been clearly capable of arriving at the claimed method.

With regard to the detection of target nucleic acids such as mRNA or RNA or cDNA derived from mRNAs, such detection method involving microarrays have long been practiced and thus one of ordinary skill in the art would have been motivated to combine the teachings of Lockhart et al. with the teachings of Hubbell et al., thereby arriving at the invention as claimed.

Therefore, the invention as claimed is *prima facie* obvious over the cited references.

Claims 37-40, 44-46, and 50-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hubbell et al. (U.S. Patent No. 6,130,046, issued October 10, 2000) in view of Fisher et al. (U.S. Patent No. 6,232,072, issued May 5, 2001).

The teachings of Hubbell et al. have already been discussed above.

Hubbell et al. do not explicitly disclose that the method be employed for inkjet fabrication of arrays.

Fisher et al. explicitly discloses that there are fabrication defects in microarrays produced by inkjet fabrication methods (column 2, lines 19-33).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Hubbell et al. and the teachings of Fisher et al., thereby arriving at the invention as claimed for the following reasons.

Hubbell et al. state that while their preferred embodiments are directed to methods that utilize VSLIP™ technology, ***explicitly state*** that their invention is **not limited to this technology**

and may be advantageously applied to other manufacturing processes." (column 3, lines 43-46; Hubbell et al.)

Fisher et al. evidences the presence of synthesis defect in microarrays produced by inkjet printing process:

> "However, every component in an array deposition apparatus are subject to errors such as component failure or variances in its operating parameters within, or sometimes even outside of, normal tolerances for such component. For example, a dispensing head used to dispense fluid droplets to form the array, may have one or more jets which fail or which vary slightly in the size of the droplets dispensed..." (column 2, lines 19-25; Fisher et al.)

Therefore, one of ordinary skill in the art would have been motivated to employ the teachings provided for by Hubbell et al. in the method of synthesizing arrays via inkjet technology for the purpose of making certain of quality of the arrays synthesized, arriving at the invention as claimed.

One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success at producing the combined invention as synthesis of microarrays via inkjet technology had been well established in the art of microarray fabrication (as evidenced by Fisher et al.). Since probes of arrays of Hubbell et al. and those of Fisher et al. are produced by monomer-by-monomer addition, one of ordinary skill in the art would have been clearly capable of adapting the method of Hubbell et al. for the method of checking the quality of arrays produced by inkjet, rendering the claimed invention *prima facie* obvious over the cited references.

Therefore, the invention as claimed is *prima facie* obvious over the cited references.

Conclusion

No claims are allowed.

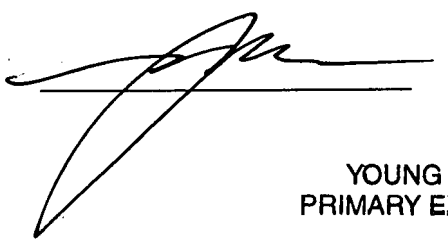
Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Young J. Kim whose telephone number is (571) 272-0785. The Examiner is on flex-time schedule and can best be reached from 8:30 a.m. to 4:30 p.m (M-W and F). The Examiner can also be reached via e-mail to Young.Kim@uspto.gov. However, the office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Gary Benzion, can be reached at (571) 272-0782.

Papers related to this application may be submitted to Art Unit 1637 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1:6(d)). NOTE: If applicant does submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office. All official documents must be sent to the Official Tech Center Fax number: (571) 273-8300. For Unofficial documents, faxes can be sent directly to the Examiner at (571) 273-0785. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



YOUNG J. KIM
PRIMARY EXAMINER

Young J. Kim
Primary Examiner
Art Unit 1637
11/25/2007

YJK